

A Randomized Controlled Trial of Patient-Reported Outcomes With Tai Chi Exercise in Parkinson's Disease

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ABSTRACT: A previous randomized, controlled trial of tai chi showed improvements in objectively measured balance and other motor-related outcomes in patients with Parkinson's disease. This study evaluated whether patient-reported outcomes could be improved through exercise interventions and whether improvements were associated with clinical outcomes and exercise adherence. In a secondary analysis of the tai chi trial, patient-reported and clinical outcomes and exercise adherence measures were compared between tai chi and resistance training and between tai chi and stretching exercise. Patient-reported outcome measures were perceptions of health-related benefits resulting from participation, assessed by the Parkinson's Disease Questionnaire (PDQ-8) and Vitality Plus Scale (VPS). Clinical outcome measures included motor symptoms, assessed by a modified Unified Parkinson's Disease Rating Scale–Motor Examination (UPDRS-ME) and a 50-foot speed walk. Information on continuing exercise after the structured interventions were terminated was obtained at a 3-month postintervention follow-up. Tai chi participants reported significantly better improvement in the PDQ-8 (−5.77 points, $P = 0.014$) than did

resistance training participants and in PDQ-8 (−9.56 points, $P < 0.001$) and VPS (2.80 points, $P = 0.003$) than did stretching participants. For tai chi, patient-reported improvement in the PDQ-8 and VPS was significantly correlated with their clinical outcomes of UPDRS-ME and a 50-foot walk, but these correlations were not statistically different from those shown for resistance training or stretching. However, patient-reported outcomes from tai chi training were associated with greater probability of continued exercise behavior than were either clinical outcomes or patient-reported outcomes from resistance training or stretching. Tai chi improved patient-reported perceptions of health-related benefits, which were found to be associated with a greater probability of exercise adherence. The findings indicate the potential of patient perceptions to drive exercise behavior after structured exercise programs are completed and the value of strengthening such perceptions in any behavioral intervention.

Key Words: exercise; patient-oriented outcomes; Parkinson's disease

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Despite increasing evidence that exercise improves motor-related symptoms of Parkinson's disease,¹⁻⁴ patient-reported outcomes, such as perceptions of mental and physical health gains, in exercise-based interventions have received little attention.⁴ With the growing emphasis on patient-reported outcomes in research and clinical practice,⁵⁻⁹ it is imperative that researchers and clinicians alike understand the value of patient perceptions of health-related quality of life and/or benefits derived from exercise, the relationship between intervention effects and patient-reported outcomes, and the impact of patient-reported perceptions resulting from exercise on exercise adherence beyond a supervised training period. Evaluating these process and outcome characteristics is important from the perspectives of: (1) understanding patient views of maintaining quality of life and managing the impact of the condition on daily life, (2) improving patient care, and (3) enhancing intervention/treatment compliance and achieving desired outcomes.

Previously, we have shown that tai chi exercise improves both laboratory and clinically assessed physical outcomes of postural control and mobility compared with either resistance training or stretching exercise.¹⁰ Utilizing secondary analysis of the data from this previously published study, the current study was intended to evaluate exercise-induced change in patient-reported outcome measures. Specifically, the primary aim was to investigate whether tai chi, a balance-based training modality, could positively affect patient perceptions of health-related benefits. Given the growing interest of public health authorities in linking patient-reported outcomes to care outcomes,⁶⁻⁸ two secondary aims were included to explore: (1) whether improvement in patient perceptions was associated with change in clinically evaluated functional outcomes and (2) the relative contribution of exercise-induced patient-reported outcomes and clinical outcomes to continuing exercise behavior during a postintervention follow-up.

Patients and Methods

Study Design and Participants

The data analyzed in this study were derived from a randomized, controlled trial that was designed to evaluate the efficacy of tai chi in improving postural stability and physical performance in patients with mild to moderate Parkinson's disease. The full design, methodology and main outcomes were reported in a previous article.¹⁰ Briefly, the study involved 3 active exercise arms (tai chi, resistance training, stretching exercise) with study participants engaged in 60-minute group exercise sessions twice weekly for 6 months. In light of the purposes of the current study, for analysis

we used 2 patient-reported outcome measures and 2 a priori selected clinical measures assessed at baseline and at the 6-month intervention termination and a measure of adherence to exercise collected at the 3-month postintervention follow-up.

The study population consisted of individuals aged 40 to 85 years with mild to moderate Parkinson's disease, as defined by the Hoehn and Yahr staging scale (range, 1-4),¹¹ recruited between May 2008 and November 2010 in 4 cities in Oregon (Eugene, Corvallis, Salem, and Portland) by means of public advertisements, referrals from health care providers, and promotion at local Parkinson's disease support groups.

Following initial screening for eligibility and baseline assessment, participants were randomized to tai chi ($n = 65$), resistance training ($n = 65$), or stretching ($n = 65$) groups. The Oregon Research Institute Institutional Review Board approved the study, and all participants gave written informed consent before enrolling in the study.

Intervention Group

Each condition received the same amount of contact time from instructors and staff during the entire trial period. Exercise instructors were certified by professional organizations such as the American College of Sports Medicine, and tai chi instructors were trained and certified by the Oregon Research Institute.

Participants in the tai chi group practiced a protocol that consisted of 6 tai chi movements integrated into an 8-form routine. Because the goal was to maintain balance through proactive postural control, the training protocol was specifically aimed at taxing balance, limits of stability, and gait by having participants perform symmetrical and diagonal movements such as weight shifting, controlled displacement of the center of mass over the base of support, ankle sways, and anterior-posterior and lateral stepping. The first 10 weeks of training emphasized mastering single forms through multiple repetitions; later weeks focused on repetitions to enhance balance and increase locomotion. Natural breathing was integrated into the training routine.

Participants in the resistance training group received training that involved movement of the legs, trunk, and arms as reflected in activities such as forward/side stepping, squats, forward/side lunges, and heel and toe raises; all were designed to improve strength, balance, and locomotion. External resistance (ie, weighted vests, ankle weights) was added in week 10. Weighted vest resistance was initially set at 1% of body weight and was increased approximately 1% to 2%, depending on each subject's tolerance, every fifth week until 5% of body weight was achieved. Ankle weights started at 0.45 kg (1 pound) per limb and were

gradually increased to 1.36 kg (3 pounds) per limb. The exercises described above were performed in 1 to 3 sets of 10 to 15 repetitions. Progression was modified on an individual basis according to ability.

Participants in the stretching group were provided with a low-impact exercise regimen that encompassed a variety of seated and standing stretches involving the upper body (neck, upper back, shoulder, chest, and arms) and lower extremities (quadriceps, hamstring/calf, and hip) using gentle joint extension/flexion and trunk rotation. Abdominal breathing that emphasized inhaling and exhaling to maximum capacity and relaxation of major muscles was also included.

Assessments

Measures were: (1) patient-reported outcomes, (2) clinically assessed outcomes, and (3) patient self-report of continuing exercise. All assessments, conducted by trained assessors who were blinded to group assignment, were performed during an in-office visit at a designated research facility. Assessments were made while participants were in “on-medication” status.

Patient-Reported Outcome Measures

Two measures assessing perceived benefits attributed to exercise participation were used: the Parkinson's Disease Questionnaire (PDQ)—the short version, PDQ-8¹²—and the Vitality Plus Scale (VPS).¹³ The PDQ-8 consists of 8 items, anchored on a 5-point Likert scale, to assess health-related quality of life involving dimensions of mobility, activities of daily living, emotional well-being, stigma, social support, cognitions, communication, and bodily discomfort. A summary score was calculated by converting the raw scores to a range from 0 (best—no problem at all) to 100 (worst—maximum level of difficulty). Reliability and validity of the PDQ-8 have been established by the developers.¹² In this study, internal consistency of the scale was 0.74. Although no universally accepted standard for establishing the minimally important difference (MID) for the PDQ-8 has been established, the anchor-based range derived from a longitudinal study by Luo et al¹⁴ was used to identify clinically relevant changes. The VPS scale consists of 10 items assessing health-related benefits of exercise participation and is designed to capture a number of interrelated aspects of “feeling good” (eg, sleep, energy level, mood) in a single instrument. The single summary VPS score ranges from 10 to 50, with higher scores representing more positive perceived benefits of exercise participation. Internal consistency of the scale obtained from this study was 0.84.

Clinical Measures

Clinical measures included 2 mobility measures: (1) a modified version of the Unified Parkinson's Disease Rat-

ing Scale Motor Examination (UPDRS-ME),¹⁵ which was reported in our prior trial¹⁰ and (2) a 50-foot speed walk test. The decision to use these 2 measures was made a priori because both core interventions (tai chi, resistance training) were designed to tax axial parkinsonian symptoms (ie, posture, postural stability) and mobility (rising from a chair, rigidity, leg agility, gait), and these measures are considered to have significant clinical relevance for patients with Parkinson's disease. The UPDRS¹⁵ was modified by collapsing each bilateral rating on the original measure into a single composite item. The resulting modified scale comprised 14 items (compared with the original 27 ratable items), each rated on a 5-point Likert scale from 0 (no impairment) to 4 (marked impairment), with a total score range of 0 to 56, with lower values indicating less motor disability. The 50-foot speed walk assessed the time it took participants to walk as quickly as possible 25 feet out and 25 feet back, recorded (in seconds), from the command “go” until the starting line was crossed on the way back.

Continuing Exercise Measure

Upon completion of the intervention, participants were encouraged to continue to exercise in any form. Information on continuing exercise during the 3-month postintervention period was collected through patient self-report data at the 3-month follow-up assessment visit. Participants reporting “exercising equal to or greater than two times per week for at least 30 minutes per session” were classified as “continuing exercise.”

Statistical Analysis

Following the gold standard in clinical trials,¹⁶ the data were analyzed on an intention-to-treat basis. Descriptive statistics (means, standard deviations) were calculated for the patient-reported outcomes. In addressing the primary aim, pre- to postchange (baseline to intervention termination) in patient-reported outcome measures of the PDQ-8 and VPS were analyzed using generalized estimating equation (GEE) with a Gaussian distribution. A similar approach was used to analyze change in the clinical measures of the UPDRS-ME and 50-foot speed walk scores.

Next, to examine the association between patient-reported (PDQ-8, VPS) and clinical (UPDRS-ME, 50-foot speed walk) outcome measures (the first secondary aim), Pearson's product-moment correlation was performed using pre- to postchange scores between the 2 pairs of continuous variables for each intervention group and on the total study population. By converting each correlation coefficient into a *z* score using Fisher's *r*-to-*z* transformation, the difference between 2 (independent) correlation coefficients under scrutiny was then tested across the intervention conditions.¹⁷

TABLE 1. Patient-reported outcome measures at baseline and 6 months (means with standard deviations) and between-group differences in change from baseline

Measure	Tai chi (n = 65)	Resistance (n = 65)	Stretching (n = 65)	Between-group difference in change from baseline to 6 months			
				Tai chi vs. resistance (95% CI)	<i>P</i>	Tai chi vs. stretching (95% CI)	<i>P</i>
PDQ-8 score ^a							
Baseline	25.14 ± 16.81	25.28 ± 14.67	25.19 ± 16.27				
6 Months	15.48 ± 11.35	21.39 ± 12.72	25.10 ± 15.55	−5.77 (−10.37 to −1.16)	0.014	−9.56 (−13.85 to −5.29)	< 0.001
VPS score ^b							
Baseline	33.52 ± 5.99	33.59 ± 5.44	33.73 ± 6.54				
6 months	36.72 ± 6.91	36.12 ± 6.86	34.14 ± 6.21	0.66 (−1.10 to 2.73)	0.528	2.80 (0.96 to 4.64)	0.003

CI, confidence interval.

^aThe PDQ-8 has a score range from 0 to 100, with higher scores representing worse health-related quality of life.^bThe VPS has a score range from 10 to 50, with higher scores representing higher levels of perceived benefits of exercise participation.

Finally, to examine the relative contribution of patient-reported outcomes and clinical outcomes to continuing exercise at the 3-month postintervention follow-up (the second secondary aim), we first dichotomized the 4 continuous variables as “improved” (1) or “not improved” (0) on the basis of pre-to-post intervention change scores using a median split method. In the subsequent logistic regression analyses, we first estimated a set of 4 models involving the main effect of the patient-reported and clinical outcomes (dichotomous predictor variables—PDQ-8, VPS, UPDRS-ME, and 50-foot speed walk) and intervention condition (a 3-level categorical predictor variable, with the dummy vectors representing resistance training and stretching) on continued exercise behavior (the binary outcome variable). Building on the main-effect analyses, we then included an interaction term in all 4 logistic regression models (in addition to the main effect for each respective patient/clinical variable and intervention) to examine the effect of improved versus not improved of each patient-report and clinical-outcome variable by intervention condition on continued exercise behavior. The full logistic model is specified using the following equation:

$$\text{Logit } (P(\text{ContinueExercise} = 1)) = B_0 + B_1 \cdot \text{Patient/ClinicalOutcome (Improved)} + B_2 \cdot \text{Intervention (Stretching)} + B_3 \cdot \text{Intervention (Resistance)} + B_4 \cdot \text{Stretching} * \text{Improved} + B_5 \cdot \text{Resistance} * \text{Improved},$$

where *P* is probability,
Bs are beta coefficients, and *B*₀ is the intercept].

Instead of presenting odds ratios in the presence of interaction terms,¹⁸ we report expected probabilities for each intervention group by improvement status defined previously. In all analyses, important demographic and clinical profile variables such as sex, age, disease stage, health status, and change in medication use and physical activity were initially controlled for.

Because inclusion of these variables had little influence on the outcome, final estimates were reported on the basis of a model that does not contain the covariates. A 2-tailed *P* < 0.05 was considered statistically significant, and all tests were conducted using Stata statistical software (version 13).

Results

As reported in our original trial,¹⁰ of 309 individuals assessed for eligibility, 195 (63%) were screened, qualified, and subsequently randomized to an intervention group. The mean age was 68.7 years, 63% of the participants were men, and 84% were classified on the Hoehn and Yahr scale at stage 2 or higher (56 in tai chi, 51 in resistance training, 57 in stretching) with a range of 1 to 4 (median, 2.5). The mean score for the modified UPDRS was 15.2 (15.28 in tai chi, 15.32 in resistance training, 15.06 in stretching). The mean age at initial diagnosis was 63.7 years, with a mean of 7.3 years since diagnosis. A total of 143 participants (73%) reported taking levodopa or carbidopa, with 53 (27%) taking pramipexole or ropinirole. The mean number of antiparkinsonian medications used was 3.5 (3.1 in tai chi, 3.2 in resistance training, 3.1 in stretching). There were no between-group differences at baseline in participant characteristics, including age, sex, duration of Parkinson's disease, Hoehn and Yahr stages, number of medications, or patient-reported and clinically measured outcomes.

Of the 195 participants, 176 (90%) completed their assigned interventions (56 in tai chi, 59 in resistance training, 61 in stretching), and 185 (95%) provided complete data on the outcome measures (61 in tai chi, 62 in resistance training, 62 in stretching). During the 24-week trial period, there were no serious adverse events reported, and there were no major changes in antiparkinsonian medications. After completion of the 6-month intervention, 123 study participants (62%) reported

TABLE 2. Pearson's correlation in change scores between patient-reported outcomes and clinically assessed outcomes for the whole study sample and across three intervention groups

	Total Study Sample			
	PDQ-8	P	VPS	P
Modified UPDRS-ME	0.31	<0.000	−0.28	<0.000
50-Foot speed walk	0.23	0.001	−0.30	<0.000

Clinical measure	Tai chi (n = 65)		Resistance (n = 65)		Stretching (n = 65)	
	PDQ-8	P	PDQ-8	P	PDQ-8	P
Modified UPDRS-ME	0.26	0.043	0.20	0.034	0.18	0.149
50-Foot speed walk	0.31	0.011	0.22	0.075	0.01	0.989
	VPS		VPS		VPS	
	PDQ-8	P	PDQ-8	P	PDQ-8	P
Modified UPDRS-ME	−0.31	0.012	−0.22	0.075	−0.15	0.234
50-Foot speed walk	−0.35	<0.000	−0.21	0.97	−0.08	0.507

continuing to exercise during the 3-month postintervention follow-up. More participants in the tai chi group ($n = 47$) continued than for either resistance training ($n = 41$) or stretching ($n = 35$) conditions ($P < 0.05$).

Descriptive information on patient-reported outcome measures at baseline and after 6 months and between-group differences in change in these measures from baseline are shown in Table 1. GEE analyses indicated a significant group by linear trend interaction ($P < 0.001$) on the 2 patient-reported outcome variables. Although both the tai chi and resistance training groups reported a significant change from baseline ($P < 0.01$), analysis showed that compared with the other 2 intervention arms, only tai chi reached the MID for the PDQ-8.¹⁴ A follow-up analysis of difference-in-difference estimators indicated that with the exception of VPS change scores between tai chi and resistance training, the change (6 months minus baseline) in the patient-reported outcomes was larger in the tai chi group compared with either resistance training (PDQ-8, -5.77 points; $P = 0.014$) or stretching (PDQ-8, -9.56 points, $P < 0.00$; VPS, 2.80 points; $P = 0.003$).

Correlation coefficients in change scores between patient-reported and clinical outcome measures for the whole study sample population and among the 3 study conditions are presented in Table 2. As can be seen, correlation coefficients were statistically significant for the whole study sample (top of Table 2). Within-group correlations results (bottom of Table 2) showed that for the tai chi group, the improvements in the PDQ-8 and VPS were significantly correlated with improvements in UPDRS-ME and 50-foot walk scores ($P < 0.01$). There was also a significant (positive) correlation ($P < 0.03$) between PDQ-8 and the modified

UPDRS-ME in the resistance training group. However, tests of the difference between these correlation coefficients indicated no statistical between-group differences (data not shown).

Table 3 presents the probabilities of continuing to exercise based on intervention group and improvement status in the patient-reported and clinical outcome measures. Logistic regression results indicated that there were significant interactions between patient-reported outcomes and intervention condition ($P < 0.05$). There was, however, no significant interaction between clinical outcomes and continuing to exercise. The significant intervention condition by patient-reported improvement status interaction effect corresponded to the differential effect of improved versus not improved across the intervention groups. Inspection of the probabilities shown in Table 3 indicates that tai chi participants reporting improved patient-reported outcomes were more likely to continue exercise during the postintervention period compared with either resistance training or stretching groups.

Discussion

This study shows that both tai chi and resistance training improved Parkinson's patient perceptions of health benefits resulting from exercise. Although improvements in patient-reported outcomes in the 2 groups were weakly correlated with improvements in clinical outcomes, the effects of improved patient-reported outcomes from tai chi were more pronounced in that they were significantly associated with continuing exercise behavior following the prescribed exercise intervention.

The findings, the first from a study involving tai chi with this clinical population, indicate improved patient-reported outcomes that parallel previous tai chi studies involving healthy, community-dwelling

TABLE 3. Estimated probabilities for each intervention group by improvement status on patient-reported and clinical outcomes^a

Intervention by improvement status	Probability of continued exercise			
	Model with PDQ-8	Model with VPS	Model with UPDRS-ME	Model with 50-foot walk
Tai chi + improved	0.80	0.80	0.67	0.60
Tai chi + not improved	0.54	0.40	0.48	0.31
Resistance + improved	0.69	0.77	0.66	0.62
Resistance + not improved	0.57	0.57	0.47	0.56
Stretching + improved	0.57	0.40	0.59	0.44
Stretching + not improved	0.45	0.30	0.42	0.21

^aDerived from each of the 4 logistic regression models involving patient-reported and clinical outcomes.

older adults that have shown improvements in self-reported well-being,^{19,20} multiple domains of self-esteem,²¹ self-efficacy/confidence in balance and movement,²² sleep quality,^{23,24} and physical function.²⁵ These findings suggest that tai chi may be prescribed as an adjunct exercise intervention to improve health-related outcomes deemed important to quality of life.

The current study also extends previous exercise-based research²⁶⁻²⁸ by exploring the relationship between patient-reported health benefits and clinically assessed outcomes and how this relation was affected by the exercise intervention delivered. Although we found clinically meaningful improvement in PDQ-8 scores and statistically significant change scores for VPS in the tai chi group, correlations between the patient-centered and clinical outcomes were small in effect size. Although this finding is consistent with observations of low or moderate relationships between patient-reported outcomes and clinical data,²⁹ it suggests that patient-reported outcomes may provide information based on different perspectives; this is an empirical issue that warrants further investigation in terms of understanding mechanisms that may underlie the patient-reported and clinical outcomes relationship in exercise-based interventions.

Finally, the results indicating that patient-reported outcomes may be more important to the likelihood of participants continuing to exercise than clinical outcomes points to some relevant aspect of perceptions that may influence exercise behavior. Thus, how patients perceive the benefits of an exercise intervention may be more potent to their motivation to continue to exercise than their actual physical/clinical status. These findings, then, underscore the value of patient-reported outcomes and suggest the need to focus on improving participant perceptions of health benefits to maximize the positive impact of exercise interventions through continued participation.

Study Limitations

The study has some limitations. First, because participants volunteered for the original study, the sample may have been subject to selection bias in that these patients may have been more motivated to participate in research activities than other persons with Parkinson's disease, therefore, not all segments of the target population may have been represented. Second, a modified UPDRS motor scale was used in this study (each bilateral rating was collapsed into a single composite score resulting in a total of 56 points rather than the standard 108 points). As a result, the motor symptoms measured in this study may not have provided a full range of motor disability as would be captured by the original full motor scores. Third, dichotomizing the continuous predictor variables based on median splits may have resulted in loss of

information or analytic power. Given that the substantive interest in this study was to understand how improvement in either patient-reported outcomes or clinically assessed outcomes predicted continued exercise, in the absence of specific guidelines on clinically meaningful cutoff points in these measures, we believe our approach was justified but should be subject to future verification. Finally, future studies would benefit from using qualitative measures that address health-related issues regarded as important by patients to develop tailored interventions.

Conclusion

Patient-centeredness has been identified as a key dimension of health care³⁰ because it is thought to improve patient-provider communication and result in higher-quality health care.³¹⁻³³ The focus on measuring patient perceptions of health-related benefits of tai chi in this study was in direct response to the emerging call for including patient viewpoints and perceptions in clinical practice and research.³² In clinical settings, satisfaction with health care has been implicated as important in understanding clinical outcomes and adherence to treatment guidelines.³⁴ Although exercise-based research on Parkinson's disease is increasing,³ few studies have focused on patient-oriented outcomes.⁴ This study addressed this issue by evaluating the link between patient-reported outcomes and clinical and behavioral outcomes. Findings suggest that perceived health-related benefits may be an important component of patient experience with exercise programs and should be a measured outcome in behavioral interventions.

In conclusion, results from this study indicate perceptions of health outcomes from participating in tai chi improved to a clinically relevant degree in patients with Parkinson's disease and that these patient-reported outcomes appear to be significantly associated with exercise adherence. Future patient-centered outcomes that incorporate assessments of tai chi training-induced positive affect experienced by patients in concert with standard clinical measures may allow us to unravel how changes that occur during treatment translate into high-quality, clinically meaningful intervention outcomes. ■

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